E. faecalis, sensitive to ampicillin and glycopeptides (vancomycin and teicoplanin), but expressing high-level gentamicin resistance. The patient was treated with a combination of intravenous ampicillin and teicoplanin (for which in vitro synergy was demonstrated) for 2 weeks followed by oral amoxycillin plus intramuscular teicoplanin for 4 weeks. She awaits assessment for the second stage of her surgery.

These patients demonstrate several of the etiologic factors which predispose to prosthetic joint infection: urologic trauma (case 1), rheumatoid arthritis and postoperative trauma (case 2). Both cases highlight the need to collect multiple specimens for culture in order to make the diagnosis and guide antimicrobial therapy. Enterococci may cause up to 10% of prosthetic joint infections and are associated with urologic or gastrointestinal procedures [1]. Enterococci are inherently resistant to the usual orthopedic perioperative antibiotic prophylaxis regimens. Until recently enterococci were predictably sensitive in vitro to combinations of ampicillin or a glycopeptide antibiotic (vancomycin, teicoplanin) with an aminoglycoside. However, the presence of high-level gentamicin resistance abolishes the potential for synergistic use of aminoglycosides [2]. More recently, both acquired ampicillin resistance and resistance to glycopeptide drugs have emerged in enterococci, leading to hospital outbreaks of multiply-resistant organisms [3]. There is currently a need for novel therapeutic approaches in order to achieve cidal antimicrobial activity against enterococci. As nosocomial infections due to these organisms, notably multiply-resistant *E. faecium*, increase, we can expect to encounter more enterococcal joint infections. The prevention of such infections requires a reconsideration of antibiotics for prophylaxis and in cement, as highlighted in recent correspondence [4], together with aggressive management of predisposing perioperative factors.

Paul R. Chadwick[1]
Naomi Davis[2]
Anthony D. Clayson[2]
Hari Panigrahi[1]
[1]Department of Microbiology,
North Manchester General Hospital,
Manchester, UK
[2]Department of Orthopaedics,
North Manchester General Hospital,
Manchester, UK;

References

1. Brause BD. Infections associated with prosthetic joints. Clin Rheumatic Dis 1986; 12: 523–36.
2. Leclercq R, Dutka-Malen S, Brisson-Noel A, et al. Resistance of enterococci to aminoglycosides and glycopeptides. Clin Infect Dis 1992; 15: 495–501.
3. Woodford N, Johnson AP, Morrison D, Speller DCE. Current perspectives on glycopeptide resistance. Clin Microbiol Rev 1995; 8: 585–615.
4. Leblebicioglu H, Sanic A, Gunaydin M, Sencan I, Dabak N, Nas Y. In-vitro release of vancomycin and netilmicin from bone cement. Clin Microbiol Infect 1996; 1: 211–13.

Treatment of disseminated *Mycobacterium simiae* infection in AIDS

Clin Microbiol Infect 1997; 3: 265–267

Mycobacterium simiae is a rare cause of human infection. It is usually considered to be a commensal in the sputum of patients with underlying pulmonary diseases [1]. Only a small percentage of immunocompetent patients have had proven clinical disease [2]. In recent years, *M. simiae* has been reported as a cause of disseminated infection in five patients with AIDS [3–6]. Two patients were co-infected with the *M. avium* (MAI) complex [4,5]. In three cases, *M. simiae* was the only microorganism isolated (from blood culture, sputum and bone marrow), clearly demonstrating the pathogenic role of *M. simiae* [3,6]. The choice of optimal therapy is unclear, and the outcome was poor in the five cases previously reported [3–6]. We report a case of disseminated *M. simiae* infection in a patient with AIDS, who was successfully treated with a combination regimen that comprised clarithromycin, sparfloxacin and cycloserine.

A 52-year-old caucasian heterosexual man was found to be HIV positive in 1989. He had a history of sexual contacts with prostitutes in Burkina Faso. He had been treated with zidovudine since October 1990 and was asymptomatic. In September 1994, after travel to Burkina Faso, he presented with fever, diarrhea and weight loss of 6 kg. His CD4 cell count was 45/mm^3. CT scans of the thorax and abdomen showed three right pulmonary parenchymal nodular opacities and retroperitoneal lymphadenopathy (1 × 2 cm). All other investigations were negative and no infective agent was detected in initial tests. He was treated empirically, for suspected disseminated MAI infection, with clarithromycin (2000 mg/day), rifabutin (600 mg/day) and ethambutol (1200 mg/day). Staining of several sputum specimens revealed acid-fast bacilli. The patient responded to this therapy within 2 weeks. Culture from blood, sputum induction and bronchoalveolar lavage yielded *M. simiae* (identified by the National Mycobacterium Reference Laboratory). Rifabutin was

discontinued because of arthralgia and ofloxacin was added. In spite of this treatment, the patient's condition deteriorated, in January 1995, with intermittent fever and weight loss. In March 1995, repeat CT scan revealed mediastinal, intra-abdominal and retroperitoneal lymphadenopathies with central cavitation (2 × 3 cm). His blood culture on this occasion was negative for *M. simiae*. The initial isolates of *M. simiae* were found to be sensitive in vitro to rifabutin and cycloserine, but resistant to clofazimine, ciprofloxacin, amikacin, ofloxacin and ethambutol. The MIC of clarithromycin was 16 μg/mL. Therapy was changed to clarithromycin (2000 mg/day), cycloserine (500 mg/day) and sparfloxacin (250 mg/day), with subsequent clinical and radiologic improvement. Cycloserine was discontinued in November 1995 because of dizziness. The patient was still alive in August 1996.

This patient was born in France but lived transiently in Burkina Faso. Among the five cases described in the literature, two patients lived in Israel [3], one patient was born in Puerto Rico and lived in New York City [5]; and two patients were born and lived in Africa (Congo [4] and Burundi [6]). The relatively high prevalence of *M. simiae* infection in the Israeli AIDS patients seems to be related to the high prevalence of this species in Israel [3]. A similar association has been reported between *M. kansasii* infection and AIDS patients from Northern Texas, an area in which this species is hyperendemic. Our patient and two cases described in the literature lived in Africa. *M. simiae* should be added to the growing list of non-tuberculous mycobacteria that infect AIDS patients, especially those who live in areas where the prevalence of this organism is high [6–8].

The diversity of mycobacterial species infecting patients with AIDS makes full identification imperative as a guide to appropriate therapy. Guidelines for chemotherapy of *M. simiae* infections suggest that the drug regimens proposed for treatment of MAI infections should be used and that antibiotic susceptibilities should be determined [8]. *M. simiae* is resistant in vitro to conventional antituberculous drugs [3,9], but appears to be susceptible to ethionamide, cycloserine, clofazimine and amikacin [10]. Unfortunately, in vivo data are limited, although combination therapy with rifampin, clofazimine and amikacin demonstrated efficacy against *M. simiae* in a murine model [11]. Recently, the activities in vitro and in vivo of newer antimycobacterial agents such as macrolides and quinolones have been studied [10] and suggest a potential role for clarithromycin and ofloxacin in the treatment of *M. simiae* infection [10]. Our patient was successfully treated with a combination regimen including clarithromycin, sparfloxacin and cycloserine, despite multiple drug resistance in vitro. He responded also to the first combination regimen that included clarithromycin, rifabutin and ethambutol. These encouraging results suggest an important role for these agents in the treatment of human *M. simiae* infections. More studies, however, are needed to determine the activities of other agents, in order to optimize therapy for this multidrug-resistant mycobacterial species.

Marie-Pierre Steineur[1], André Boibieux[2], Thierry Zenone[1], Gilles Chaumentin[1], Bénédicte Contamin[1], Bénédicte Druel[3], Sylvestre Tigaud[3], Véronique Vincent[4], Dominique Peyramond[1]

[1]Department of Infectious and Tropical Diseases, Hôpital de la Croix-Rousse, Lyon, France; [2]Service des Maladies Infectieuses et Tropicales, Hôpital de la Croix-Rousse, 93, Grande rue de la Croix-Rousse, 69 317 Lyon Cedex 04 France; [3]Microbiology Laboratory, Hôpital de la Croix-Rousse, Lyon, France; [4]National Mycobacterium Reference Laboratory, Institut Pasteur, Paris, France

References

1. Bell RC, Higuchi JH, Donovan WN, Krasnow I, Johanson WG. *Mycobacterium simiae*. Clinical features and follow-up of twenty-four patients. Am Rev Respir Dis 1983; 127: 35–8.
2. Rose HD, Dorff GJ, Lauwasser M, Sheth NK. Pulmonary and disseminated *Mycobacterium simiae* infection in humans. Am Rev Respir Dis 1982; 126: 1110–13.
3. Huminer D, Dux S, Samra Z, et al. *Mycobacterium simiae* in Israeli patients with AIDS. Clin Infect Dis 1993; 17: 508–9.
4. Lévy-Frébault V, Pangon B, Buré A, Katlama C, Marche C, David HL. *Mycobacterium simiae* and *Mycobacterium avium-M. intracellulare* mixed infection in acquired immune deficiency syndrome. J Clin Microbiol 1987; 25: 154–7.
5. Torres RA, Nord J, Feldman R, LaBombardi V, Barr M. Disseminated mixed *Mycobacterium simiae–Mycobacterium avium* complex infection in acquired immunodeficiency syndrome. J Infect Dis 1991; 164: 432–3.
6. Vandercam B, Gala J, Vandeweghe B, et al. *Mycobacterium simiae* disseminated infection in a patient with acquired immunodeficiency syndrome. Infection 1995; 23: 1–3.
7. Schroder KH, Kazda J, Muller K, Muller HJ. Isolation of *Mycobacterium simiae* from the environment. Int J Med Microbiol Virol Parasitol Infect Dis 1992; 277: 561–4.
8. Falkinham III JO. Epidemiology of infection by nontuberculous mycobacteria. Clin Microbiol Rev 1996; 9: 177–215.
9. Weiszfeiler JG, Karasseva V, Karczag E. *Mycobacterium simiae* and related mycobacteria. Rev Infect Dis 1981; 3: 1040–5.
10. Valero G, Moreno F, Graybill JR. Activities of clarithromycin, ofloxacin, and clarithromycin plus ethambutol against *Mycobacterium simiae* in murine model of disseminated infection. Antimicrob Agents Chemother 1994; 38: 2676–7.

11. Watson SR, Auclair LK, Collins FM. The effect of combined chemotherapy on suppressor T-cell activity in *Mycobacterium simiae*-infected mice. Immunology 1981; 43: 459–65.

Lyme disease presenting as prolonged pyrexia of unknown origin

Clin Microbiol Infect 1997; 3: 267–268

Borreliosis includes within its definition both relapsing fever and Lyme disease. Relapsing fever has been recognized in our province since at least the 1930s [1] and is thought to be caused by *Borrelia hermsii*, which is transmitted by the soft tick *Ornithodoros hermsii*. Anecdotes of relapsing fever are reported on an almost yearly basis in British Columbia and Alberta, although few of these cases are published [2], and one of the largest recognized outbreaks of tick-borne relapsing fever in North America was recognized in the Browne Mountain area of Washington state, in close proximity to the British Columbia–Washington border [3]. In addition, Lyme disease has been recognized among British Columbians, although travel to other endemic areas is a feature in the history of most patients. Whereas the clinical manifestations of Lyme disease are now well detailed for both children and adults [4,5], a relapsing fever pattern or prolonged fever of unknown origin have not been published in the pediatric medical literature. We here describe an illness consisting of prolonged fever of unknown origin which developed in a child who acquired an endemic *Borrelia burgdorferi* infection in British Columbia.

A 13-month-old-female from central British Columbia developed a right forearm rash 2 weeks after an expedition to a lake in central British Columbia in late June. The parents recalled an 'insect bite' at the site of the dermatopathy, although a specific insect could not be defined. The rash was described as having a pale center and a red expanding circular edge. Coincident with the disappearance of the rash after 3–4 weeks, a fever developed and was measured maximally at approximately 40°C orally. The child received oral amoxycillin during the time when the fever persisted but appeared to have a moderate anaphylactoid reaction consisting of rash and listlessness. Although an antibiotic allergy was considered, the child had received oral amoxycillin on one occasion previously without side effects. The patient subsequently received oral cotrimoxazole and the febrile illness resolved over 2 weeks. On a weekly basis thereafter, however, and for the 6 subsequent months, the fever recurred, lasting for 1–3 days and reaching 38–39°C orally. The febrile episodes were commonly accompanied by nausea and transient diarrhea. During this interval, the patient received several antibiotic courses, including cotrimoxazole and cefaclor for presumed urinary tract and middle ear infections. Antibiotic use, however, did not seem to affect the subsequent reappearance of the febrile illness. Although the forearm rash had completely disappeared without local residua, both legs and arms developed areas of eczematoid rash.

Laboratory data during the weekly illnesses were generally not helpful in providing a diagnosis, although two immunofluorescence antibody (IFA) titers to *B. burgdorferi* were both recorded as 1/256, at 2 and 3 months after the onset of illness. The family history was considerably complicated by the diagnosis of an inherited mitochondrial disorder in the father (including cardiomyopathy) and two siblings. Furthermore, the mother had recurrent urinary tract infection and the father required a right nephrectomy because of a complicated ureteral obstruction. There was no history of travel outside British Columbia.

The child was admitted to our children's hospital 6 months after the onset for investigation of the fever recurrences and an apparent failure to thrive in the context of the familial history of metabolic disease. A change in weight from 50th percentile (birth) to 5th percentile was observed. The child was afebrile at the time of admission and the last febrile episode had ceased 2 days before. Physical examination could not determine a focus for infection. There was no evidence of joint, central nervous system or cardiac disease. Laboratory investigations revealed: white blood cell (WBC) 10.0×10^9/L (60% lymphocytes), hemoglobin 112 g/L, and platelets 300×10^9/L. Serum electrolytes, creatinine, lactate, liver and muscle enzyme profiles and amino acids were within the normal range. Both electrocardiogram and echocardiogram were normal. A repeat of the *B. burgdorferi* serology once again revealed an IFA titer of 1/256. An IFA titer to *B. hermsii* was less than 1/128. Western blot serology using *B. burgdorferi* antigen demonstrated immune recognition of seven polypeptides in addition to the flagellar (41 kDa), OspA and OspB antigens.

Fever was not recorded during 5 days in hospital but returned 7 days later and again recurred on a weekly basis. Oral erythromycin was administered by the seventh month and continued for 10 days. The child was afebrile during the antibiotic course and has remained so after cessation of the same, apart from a single episode of fever associated with a urinary tract infection. The eczematoid rash disappeared after the erythromycin treatment and has not recurred.